ABSTRACT

The present invention is based on an *in vivo* animal model that mimics human cellular and tissue degenerative disorders. The animal model exhibits cellular toxicity in response to expanded polyglutamine repeat sequences. The animal model is therefore useful for identifying genes or other compounds that modulate cellular and tissue degeneration and cell survival, for example, in neural, muscle, mesoderm, kidney and other tissues associated with frontotemporal dementia, prion diseases, polyglutamine disorders and protein aggregation disorders. Genes that suppress degeneration identified using the animal model include HDJ1, TPR2 and MLF. These genes, and their human homologues, functional fragments and probes are therefore useful in treating such disorders and for diagnostic purposes. Accordingly, methods for identifying nucleic acids and other compounds that modulate frontotemporal dementia, prion diseases, polyglutamine disorders and protein aggregation disorders is therefore provided. Pharmaceutical compositions comprising HDJ1, TPR2 and MLF genes, and subsequences encoding functional polypeptides are also provided, as they are useful in treating such degenerative disorders.